## I. AMENDMENTS TO THE CLAIMS

**Claim 1 (Withdrawn).** A method of screening for a modulator of Mre11 comprising:

(a) contacting candidate modulators with Mre11 in vitro in the presence of a nucleic acid substrate for Mre11; and

(b) measuring the hydrolysis of said substrate, whereby a modulator is identified by altering hydrolysis of said substrate compared to a control.

**Claim 2 (Withdrawn).** The method of claim 1 wherein said nucleic acid substrate is an oligonucleotide with at least 50% nucleotide sequence identity with $(TTAGGG)_n$, wherein n=1 to 20.

**Claim 3 (Withdrawn).** The method of claim 1 wherein hydrolysis of said nucleic acid substrate is measured by UV absorbance or release of a radiolabel.

**Claim 4 (Withdrawn).** A method of screening for an agent that specifically binds to Mre11 comprising:

(a) contacting candidate agents with Mre11; and

(b) determining whether a candidate agent specifically binds to Mre11.

**Claim 5 (Withdrawn).** The method of claim 4 wherein Mre11 is attached to a solid support.

**Claim 6 (Withdrawn).** A method of screening for a modulator of Mre11 comprising:

(a) providing a cell that expresses Mre11;

(b) contacting candidate modulators with said cell under conditions in which the modulator is taken up by the cell; and

(c) measuring a property of said cells selected from the group consisting of cellular proliferation, cellular viability, cellular morphology, SA-β-Gal activity and phosphorylation of p53 or p95, whereby a modulator is identified by altering said property compared to a control.

**Claim 7 (Withdrawn).** The method of claim 6 wherein said candidate modulators specifically bind to Mre11.

**Claim 8 (Withdrawn).** The method of claim 6 wherein said Mre11 is a fragment.

homolog, analog or variant of Mre11.

**Claim 9 (Withdrawn).** The method of claim 8 wherein said fragment, homolog, analog or variant of Mre11 has exonuclease activity.

**Claim 10 (Withdrawn).** The method of claim 6 wherein the property of said cell is cellular proliferation.

**Claim 11 (Withdrawn).** The method of claim 6 wherein the property of said cell is cellular viability.

**Claim 12 (Withdrawn).** The method of claim 6 wherein the property of said cell is cellular morphology.

**Claim 13 (Withdrawn).** The method of claim 6 wherein the property of said cell is SA-β-Gal activity.

**Claim 14 (Withdrawn).** The method of claim 6 wherein the property of said cell is phosphorylation of p53 or p95.

**Claim 15 (Withdrawn).** The method of claim 6 wherein said cell is a cancer cell.

**Claim 16 (Withdrawn).** The method of claim 15 wherein the telomeres of said cell are maintained by telomerase reverse transcriptase or the ALT pathway.

**Claim 17 (Withdrawn).** The method of claim 8 wherein said cell is a cancer cell.

**Claim 18 (Withdrawn).** The method of claim 17 wherein the telomeres of said cell are maintained by telomerase reverse transcriptase or the ALT pathway.

**Claim 19 (Withdrawn).** The method of claim 15 wherein said candidate modulators are selected from the group consisting of carbohydrates, monosaccharides, oligosaccharides, polysaccharides, amino acids, peptides, oligopeptides, polypeptides, proteins, nucleosides, nucleotides, oligonucleotides, polynucleotides, lipids, retinoids, steroids,

glycopeptides, glycoproteins, proteoglycans, and small organic molecules.

**Claim 20 (Withdrawn).** The method of claim 19 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

**Claim 21 (Withdrawn).** The method of claim 17 wherein said candidate modulators are selected from the group consisting of carbohydrates, monosaccharides, oligosaccharides, polysaccharides, amino acids, peptides, oligopeptides, polypeptides, proteins, nucleosides, nucleotides, oligonucleotides, polynucleotides, lipids, retinoids, steroids, glycopeptides, glycoproteins, proteoglycans, and small organic molecules.

**Claim 22 (Withdrawn).** The method of claim 21 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

**Claim 23 (Withdrawn).** A method of screening for modulator of tankyrase comprising:

(a) contacting candidate modulators with tankyrase in vitro in the presence of a substrate for tankyrase; and

(b) measuring the ribosylation of said substrate, whereby a modulator is identified by altering ribosylation of said substrate compared to a control.

**Claim 24 (Withdrawn).** The method of claim 23 wherein said substrate is a peptide or polypeptide.

**Claim 25 (Withdrawn).** The method of claim 24 wherein said substrate is TRF1.

**Claim 26 (Withdrawn).** The method of claim 23 wherein ribosylation of said substrate is measured by UV absorbance or labeling of said substrate.

**Claim 27 (Withdrawn).** A method of screening for an agent that specifically binds to tankyrase comprising:

(a) contacting candidate binders with tankyrase; and

(b) determining whether a candidate agent specifically binds to tankyrase.

**Claim 28 (Withdrawn).** The method of claim 27 wherein tankyrase is attached to a

solid support.

**Claim 29 (Withdrawn).** A method of screening for modulator of tankyrase comprising:

(a) providing a cell that expresses tankyrase;

(b) contacting candidate modulators with said cell under conditions in which the modulator is taken up by the cell; and

(c) measuring a property of said cells selected from the group consisting of cellular proliferation, cellular viability, cellular morphology, SA-β-Gal activity and phosphorylation of p53 or p95, whereby a modulator is identified by altering said property compared to a control.

**Claim 30 (Withdrawn).** The methods of claim 29 wherein said candidate modulators specifically bind to tankyrase.

**Claim 31 (Withdrawn).** The method of claim 23 wherein said tankyrase is a fragment, homolog, analog or variant of tankyrase that has ribosylation activity.

**Claim 32 (Withdrawn).** The method of claim 31 wherein said fragment, homolog, analog or variant of tankyrase has ribosylase activity.

**Claim 33 (Withdrawn).** The method of claim 29 wherein the property of said cell is cellular proliferation.

**Claim 34 (Withdrawn).** The method of claim 29 wherein the property of said cell is cellular viability.

**Claim 35 (Withdrawn).** The method of claim 29 wherein the property of said cell is cellular morphology.

**Claim 36 (Withdrawn).** The method of claim 29 wherein the property of said cell is SA-β-Gal activity.

**Claim 37 (Withdrawn).** The method of claim 29 wherein the property of said cell is phosphorylation of p53 or p95.

**Claim 38 (Withdrawn).** The method of any of claim 37 wherein said cell is a cancer cell.

**Claim 39 (Withdrawn).** The method of claim 38 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

**Claim 40 (Withdrawn).** The method of claim 31 wherein said cell is a cancer cell.

**Claim 41 (Withdrawn).** The method of claim 40 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

**Claim 42 (Withdrawn).** The method of claim 38 wherein said candidate modulators are selected from the group consisting of carbohydrates, monosaccharides, oligosaccharides, polysaccharides, amino acids, peptides, oligopeptides, polypeptides, proteins, nucleosides, nucleotides, oligonucleotides, polynucleotides, lipids, retinoids, steroids, glycopeptides, glycoproteins, proteoglycans, and small organic molecules.

**Claim 43 (Withdrawn).** The method of claim 42 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

**Claim 44 (Withdrawn).** The method of claim 40 wherein said candidate modulators are selected from the group consisting of carbohydrates, monosaccharides, oligosaccharides, polysaccharides, amino acids, peptides, oligopeptides, polypeptides, proteins, nucleosides, nucleotides, oligonucleotides, polynucleotides, lipids, retinoids, steroids, glycopeptides, glycoproteins, proteoglycans, and small organic molecules.

**Claim 45 (Withdrawn).** The method of claim 44 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

**Claim 46 (Withdrawn).** A method of screening for a modulator of MRN complex formation comprising:

(a) contacting candidate modulators with Mre11, Rad50 and Nbs1 in vitro; and

(b) measuring the formation of the MRN complex, whereby a modulator is identified by altering formation of the MRN complex compared to a control.

**Claim 47 (Withdrawn).** The method of claim 46 wherein candidate modulators are contacted with Mre11, Rad50 and Nbs1 in the presence of a nucleic acid substrate or inhibitor of Mre11.

**Claim 48 (Withdrawn).** The method of claim 47 wherein said nucleic acid is an oligonucleotide with at least 50% nucleotide sequence identity with $(TTAGGG)_n$, wherein n=1 to 20.

**Claim 49 (Withdrawn).** The method of claim 46 wherein formation of the MRN complex is measured by centrifugation, coprecipitation or nondenaturing electrophoresis.

**Claim 50 (Withdrawn).** A method of screening for a modulator of the DNA damage pathway comprising:

(a) providing a cell that expresses Mre11 and tankyrase;

(b) contacting candidate modulators with said cell in the presence of an oligonucleotide under conditions in which the modulator is taken up by the cell; and

(c) measuring a property of said cells selected from the group consisting of cellular proliferation, cellular viability, cellular morphology, SA-β-Gal activity and phosphorylation of p53 or p95, whereby a modulator is identified by altering said property compared to a control, wherein said oligonucleotide has at least 50% nucleotide sequence identity with $(TTAGGG)_n$, wherein n=1 to 20.

**Claim 51 (Withdrawn).** The method of claim 50 wherein said Mre11 is a fragment, homolog, analog or variant of Mre11.

**Claim 52 (Withdrawn).** The method of claim 51 wherein said fragment, homolog, analog or variant of Mre11 has exonuclease activity.

**Claim 53 (Withdrawn).** The method of claim 50 wherein said tankyrase is a fragment, homolog, analog or variant of tankyrase.

**Claim 54 (Withdrawn).** The method of claim 53 wherein said fragment, homolog, analog or variant of tankyrase has ribosylation activity.

**Claim 55 (Withdrawn).** The method of claim 50 wherein the property of said cell is cellular proliferation.

**Claim 56 (Withdrawn).** The method of claim 50 wherein the property of said cell is cellular viability.

**Claim 57 (Withdrawn).** The method of claim 50 wherein the property of said cell is cellular morphology.

**Claim 58 (Withdrawn).** The method of claim 50 wherein the property of said cell is SA-β-Gal activity.

**Claim 59 (Withdrawn).** The method of claim 50 wherein the property of said cell is phosphorylation of p53 or p95.

**Claim 60 (Withdrawn).** The method of claim 59 wherein said cell is a cancer cell.

**Claim 61 (Withdrawn).** The method of claim 61 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

**Claim 62 (Withdrawn).** The method of claim 50 wherein said candidate modulators are selected from the group consisting of carbohydrates, monosaccharides, oligosaccharides, polysaccharides, amino acids, peptides, oligopeptides, polypeptides, proteins, nucleosides, nucleotides, oligonucleotides, polynucleotides, lipids, retinoids, steroids, glycopeptides, glycoproteins, proteoglycans, and small organic molecules.

**Claim 63 (Withdrawn).** A method of treating cancer comprising administering to a subject in need of such treatment a composition comprising an activator of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

**Claim 64 (Withdrawn).** A method of inducing apoptosis comprising administering to a subject in need of such treatment a composition comprising an activator of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

**Claim 65 (Withdrawn).** A method of inducing cellular senescence comprising administering to a subject in need of such treatment a composition comprising an activator of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

**Claim 66 (Withdrawn).** A method of inhibiting tanning comprising administering to a subject in need of such treatment a composition comprising an activator of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

**Claim 67 (Withdrawn).** A method of promoting cellular differentiation comprising administering to a subject in need of such treatment a composition comprising an activator of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

**Claim 68 (Withdrawn).** A method of promoting immunosuppression comprising administering to a subject in need of such treatment a composition comprising an activator of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

**Claim 69 (Withdrawn).** The method of claim 68 wherein the activator is an oligonucleotide activator of Mre11 with at least 50% nucleotide sequence identity with $(TTAGGG)_n$ and at least the first x 3'-nucleotide linkages are hydrolyzable by a 3' to 5' nuclease, wherein n=1 to 20, and wherein x is from about 1 to about 10.

**Claim 70 (Withdrawn).** A method of inhibiting apoptosis comprising administering to a subject in need of such treatment a composition comprising an inhibitor of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

**Claim 71 (Withdrawn).** A method of inhibiting cellular senescence comprising administering to a subject in need of such treatment a composition comprising an inhibitor of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

**Claim 72 (Withdrawn).** A method of promoting growth comprising administering to a subject in need of such treatment a composition comprising an inhibitor of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

**Claim 73 (Withdrawn).** A method of promoting tanning comprising administering to a subject in need of such treatment a composition comprising an inhibitor of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

**Claim 74 (Withdrawn).** A method of inhibiting cellular differentiation comprising

administering to a subject in need of such treatment a composition comprising an inhibitor of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

**Claim 75 (Withdrawn).** A method of reducing cancer treatment side effects comprising administering to a subject in need of such treatment a composition comprising an inhibitor of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

**Claim 76 (Withdrawn).** The method of claim 75 wherein the composition is given in combination with chemotherapy or ionizing radiation.

**Claim 77 (Withdrawn).** The method of claim 76 wherein the inhibitor is an oligonucleotide inhibitor of Mre11 with at least 50% nucleotide sequence identity with $(TTAGGG)_n$ and at least the first x 3'-nucleotide linkages are hydrolyzable by a 3' to 5' nuclease, wherein n=1 to 20, and wherein x is from about 0 to about 10.

**Claim 78 (Original).** A composition comprising an oligonucleotide with at least 50% nucleotide sequence identity with $(TTAGGG)_n$ and at least one nonhydrolyzable internucleotide linkage, wherein at least the first x 3'-nucleotide linkages are hydrolyzable by a 3' to 5' nuclease, wherein n=1 to 20, and wherein x is from about 0 to about 10.

**Claim 79 (Original).** The composition of claim 78 wherein the 3' to 5' nuclease is Mre11.

**Claim 80 (Original).** The composition of claim 78 wherein the oligonucleotide has at least 50% nucleotide sequence identity with TTAGGG.

**Claim 81 (Currently Amended).** The composition of claim 80 wherein the oligonucleotide ~~**or thereof has the sequence**~~ **is** GTTAGGGTTAG.

**Claim 82 (Original).** The composition of claim 78 wherein the nonhydrolyzable linkage is a phosphorothioate.

**Claim 83 (Canceled).**

The composition of claim 78 wherein the oligonucleotide is a PNA.